https://doi.org/10.55453/rjmm.2025.128.3.2

REVIEW

# Asymptomatic Bacteriuria – A Permanent Challenge in Clinical Practice: When Should We Treat It?

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**Abstract**: Asymptomatic bacteriuria (ABU) is a common finding in everyday clinical practice. Many patients, many of them with significant comorbidities, will present, when tested, with bacterial colonization of the urine even if they have no lower urinary tract symptoms at all. Therefore, the clinician is having a dilemma: Should I prescribe antibiotics to sterilize the urine or not? This article aims to update and eventually support physicians in the difficult decision of whether to treat or not to treat patients with ABS and when.

**Keywords**: asymptomatic bacteriuria, urinary tract infections, antibiotics, pregnant women, elderly patients

## INTRODUCTION

Bacterial infections represent a serious health problem worldwide [1]. The growth of bacteria in the urine of a patient who has no symptoms is named as asymptomatic bacteriuria (ABU). ABU is quite a common finding in clinical practice and corresponds to a commensal colonization of the urinary tract [2]. Enterobacterales, B Streptococcus group, and gram-negative bacilli are often met in the urine of ABU patients [3]. Among these species, Escherichia coli, followed by Klebsiella sp, were frequently detected in ABU-urine patients [3-5]. Studies have reported ABU may potentially protect against superinfecting organisms that can determine urinary tract infections (UTIs), therefore the treatment of ABU should be offered only to selected patients. Avoiding unnecessary antibiotic treatment in a significant number of patients with ABU is highly likely to avoid the potential risk of acquired antimicrobial resistance and the risk of removing a potentially effective defense mechanism [4,5]. On the other hand, in some categories of patients, the treatment of ABU proved to be beneficial, avoiding possible serious complications, some of them life-threatening like urosepsis. ABU is quite common in everyday practice. It can be identified in healthy pre-menopausal women(1-5%), with the incidence increasing to 4-19% in postmenopausal women. The ABU varies between 0.7 and 27% in diabetic patients, up to 10% in pregnant patients, and impressive rates varying between 15 and 50% are found in patients living in care homes, and in those who have had spinal cord injuries between 23 and 89% [6]. The bacteria identified in patients with ABU are not different than those found in patients with symptomatic uncomplicated or complicated UTIs.

**Citation**: Turcu FL, Vacaroiu IA, Mitrea AR, Georgescu DE, Mititelu MR, Stanigut AM, Balcangiu-Stroescu AE. *Asymptomatic Bacteriuria – A Permanent Challenge in Clinical Practice: When Should We Treat It?*. R. J. Mil. Med. 2025, 128(3): 182-187; https://doi.org/10.55453/rjmm.2025.128.3.2

**Academic Editor**: Octavian Vasiliu

**Received**: 20 December 2024
**Revised**: 12 February 2025
**Accepted**: 11 March 2025

## DISCUSSIONS

### ABU diagnosis

By definition, ABU is characterized by a mid-stream urine sample (MSU) culture with a bacterial growth of more than 105 colony-forming units/mL in a patient without any urinary tract symptoms. Two consecutive samples should be positive in female patients and only one in males [7,8].

No further investigations are required if the history is unremarkable. However, if the urine cultures confirm the presence of urease-producing bacteria, an ultrasound of the kidneys and urinary tract might be performed to rule out the urinary tract stones [8,9]. Digital rectal examination (DRE) needs to be performed in men to exclude the risk of prostate pathology, either infectious or benign/malignant. In selected cases, cystoscopy, either flexible or rigid, can offer a significant diagnostic or sometimes even treatment benefit when bladder wash-out, biopsies, or bladder stone laser disintegration is needed.

**ABU management in patients with no identified risk factors**

Studies have shown that ABU by itself in patients without any risk factors does not cause any urinary tract infections, or renal disease and does not determine acute or chronic pyelonephritis that can potentially alter the kidney function [10].

One study investigated the value of antibiotic treatment in adult, non-diabetic, non-pregnant women with ABU the incidence of symptomatic UTI was similar in both treated and not treated groups[4]. It was concluded that screening for ABU and the antibiotic treatment of ABU are not routinely recommended in patients with no risk factors and no lower urinary tract symptoms.

A study published in 2012 reviewed the ABU treatment in women with recurrent symptomatic UTIs otherwise healthy and demonstrated an increased risk of symptomatic UTIs in treated patients, compared to non-treated ones. This observation proves that ABU can play a prophylactic role in female patients with recurrent UTIs. Hence the treatment of ABU is not recommended in patients with no risk factors[5].

**ABU management in pregnant women**

ABU is present in pregnant women in between 2 to 10% of cases. Many studies were dedicated to this category of complex patients when potentially both the mother and the fetus can be affected.

A couple of RCTs [9,10] have been performed on pregnant women trying to identify if ASB treatment is needed or not. Those RCTs compared the groups with ABU treated with antibiotics versus placebo and versus no-treatment patients, also using various antibiotics and regimens. Therefore, these trials reported that the antibiotic treatment has significantly reduced the number of symptomatic UTIs in this group, versus placebo or no treatment ones. Another conclusion of these trials was that the ABU treatment has significantly decreased the rates of low birth weight and the rates of preterm delivery.

Other authors have remarked that the ABU treatment in pregnant women induces decreased incidence of symptomatic UTIs, pyelonephritis, and low birthweight or preterm delivery [11-14]. In conclusion, it seems that it is beneficial for both mother and fetus if the screening for ABU is used in pregnant women and, if bacterial growth is found in the urine, the patients should be subsequently treated appropriately. On the other hand, considering the variety and complexity of pregnant women as patients, it is always advisable to consult national guidelines and recommendations but also to consider each patient on a case-by-case basis.

As it seems that the ABU treatment in pregnant women is generally accepted, another question is which antibiotics and for how long should be used in pregnancy. A significant number of randomized clinical trials have been performed trying to answer these questions. [11-21]. These trials essentially compared different antibiotics, different regimens, or the same antibiotic prescribed in different doses or various durations. Many antibiotics have been used including mainly Nitrofurantoin, Sulphamethopirazine, Pivmecillinam, Amoxicillin, Amoxicillin associated with Clavulanic Acid, Cephalexin, Co-trimoxazole, Fosfomycin [13-15, 17, 18]. Different treatment groups were identified and used for comparison when the treatment length was considered: single dose; short course varying from 2 days to 7 days); long course considered between 8 and 14 days; and long-term course until delivery [17-20]. The data showed that single-dose treatment determined fewer side effects but more babies with low birth weight compared with the short course of treatment.

The value of Fosfomycin single dose was reviewed in a meta-analysis which compared the use of it in pregnant women with uncomplicated UTIs or ABU versus short-term courses of treatment with various antibiotics. The successful treatment of ABU was found to be not significantly different between the patients who received short-term courses of antibiotics, whatever the antibiotic used was. It was also apparent that both standard short-course treatment with various antibiotics and single dose Fosfomycin could be effective options in treating ABU in pregnant patients; however, further studies are needed [21,22].

**ABU management in patients with identified risk factors- Diabetes Mellitus**

If in 2019, worldwide 463 million people were diagnosed with diabetes mellitus (DM), in 2045 the number can increase to 700 million [23]. Long-term hyperglycemia induces several side effects affecting the eyes, nervous system, kidneys, cardiovascular disorders, [24], and periodontal disease [25]. Therefore, the diabetic patient has an increased risk of developing ABU. Even if diabetes is well controlled with the appropriate medication and diet, a significant proportion of cases with ABU [26]. A randomized control trial was addressed to these patients and found that the ABU treatment, with consecutive negative mid-stream urine, did not reduce the risk of symptomatic UTIs or pyelonephritis. On the other hand, the lack of ABU antibiotic treatment did not correlate with an increased risk of developing diabetic nephropathy [27]. It is now accepted that the ABU screening and treatment in well-controlled DM patients is not routinely recommended.

However, poorly controlled diabetes represents a significant risk factor for various infectious complications. In these patients, the doctors and nurses should make every effort to get the diabetes controlled using both medication and diet. If ABU and infectious complications are present, sounds sensible to not only treat the ABU but also further investigate these patients to rule out urological

causes.

**ABU management in patients with identified risk factors – Postmenopausal women**

Another category of patients who have an increased incidence of ABU is represented by postmenopausal women. Randomized control trials were addressed to these patients and compared the groups with ABU antibiotic treatment vs the placebo or no treatment groups, using different antibiotics and regimens [28]. There were no reported benefits of antibiotic treatment regarding both the incidence rate of symptomatic UTIs and the incidence of bacteriuria resolution [29, 30]. Therefore, as currently there is no demonstrated benefit of ABU antibiotic treatment in post-menopausal women, ASB should be managed the same in both pre-menopausal and post-menopausal women and the screening and treatment of ABU are not recommended.

**ABU management in patients with identified risk factors –Elderly/institutionalized patients**

Studies have revealed that in elderly institutionalized patients, the rate of ABU is significantly elevated, varying between 15% to 50% [4,5]. Considering that the differential diagnosis between ABU and UTIs is extremely difficult or even impossible in bed-bound, poor mobility patients who also have multiple comorbidities and are potentially mentally deteriorated, it seems that unfortunately unnecessary antibiotic treatments are prescribed in a significant number of patients [30, 31].

An important number of randomized control trials were addressed to the elderly patient population (either institutionalized or not). They were divided into three groups and the group in whom they were treated with antibiotics (different antibiotics, different doses, and regimens were prescribed), was compared with placebo controls or no-treatment groups [30-34]. These RCTs reported that the ABU treatment did not show any significant benefit, compared to placebo or no treatment groups, in reducing the rate of symptomatic UTIs. Also, there was no reported benefit of the antibiotic treatment versus placebo in obtaining a persistently negative MSU culture and sensitivity. One randomized control study compared the incidence of urinary incontinence before and after the resolution of ABU and found no effect in the group of patients who were treated with antibiotics. Even more, other studies reported that the antibiotic treatment of ABU determined significant side effects without any clinical benefit [34]. Therefore, based on the current scientific literature, we can conclude that the screening and treatment of ASB are not recommended in this group.

**ABU management in patients with identified risk factors - Renal Transplant Patients**

Renal transplant patients represent a very important category, as they are complex patients with associated pathology and sophisticated medication frequently [35-38]. A meta-analysis including randomized control trials and retrospective studies compared the effect of antibiotic treatment to no treatment in renal transplant patients and did not find any benefit in decreasing the risk of symptomatic UTIs between 12 and 22 months after transplant. No benefit was reported in ABU resolution, graft loss, or renal function preservation for up to 24 months [38].

Other publications reported that the incidence of UTIs and pyelonephritis (15% vs. 2.5%) was higher in patients receiving antibiotic treatment for ABU compared to no treatment group [37]. In another RCT, in the first year after transplantation, no difference in the acute graft pyelonephritis was found, but, not surprisingly, the incidence of antimicrobial resistance was higher in the treatment group [36]. Therefore, routine screening and treatment are not routinely recommended in patients who had renal transplantation.

**ABU management in patients with identified risk factors – Patients with dysfunctional or reconstructed lower urinary tract**

Patients with dysfunctional or reconstructed lower urinary tracts become frequently colonized having ABU [39, 40]. A study reported that the incidence of ABU varies from 25 to 86% for intestinal urinary conduits and from 9.1 to 85% for orthotopic neobladders. It has demonstrated no long-term benefit of ABU treatment in this group [40]. Interestingly, the deliberate colonization with an ABU strain (Escherichia coli 83972) has shown a protective effect against symptomatic UTI recurrences [41]. ABU screening and treatment in these patients is therefore generally not recommended.

**ABU management in patients with identified risk factors –Patients with urethral/suprapubic catheters, nephrectomies, or ureteral stents**

Patients with urethral or suprapubic catheters and nephrostomy tubes routinely become colonized with bacteria and is generally accepted nowadays that antibiotic treatment is not needed as determines no benefit. No screening for ABU or antibiotic treatment is recommended for patients with indwelling ureteral stents. Hence routine antibiotics for ABU are not recommended, as offer no benefit and determine a significant risk of acquired antibiotic resistance.

In patients who need routine urethral/suprapubic catheter changes, there is no need to be screened for ABU or to have antibiotics. On the other hand, in patients subjected to nephrostomy tube replacement or ureteral stent change, ABU is a risk factor, and therefore prophylactic antibiotics or treatment of ABU are needed [42,43].

**ABU management in patients with identified risk factors – Chronic Kidney Disease (CKD)**

Worldwide, kidney failure represents another serious complication, especially among diabetic patients [44]. Studies reported an incidence between 9-20% of UTI among female DM patients, while for male DM patients, the incidence is between 3-11% [45].

Patients with CKD are another group in whom ABU can be present. There is no study to investigate if ABU is identified in patients with CKD needs to be treated or not. As it seems that in this group there is an increased risk of antimicrobial resistance, highly likely no routine screening and treatment is needed [46]. This physician should not forget that, if treatment is needed, then it will be necessary

to prescribe the antibiotics in renal dose, considering the patients' kidney function test.

**ABU Treatment options**

If the clinician decides to treat ABU, the same antibiotics, regimens, and duration as in uncomplicated UTIs can be offered, depending on multiple characteristics like gender, co-morbidities, risk factors, allergy status, other medication the patient is taking, potential medication interactions, etc. Treatment should be always tailored on a case-by-case approach based on mid-stream urine culture and sensitivity and should not be empirical.

## CONCLUSION

ABU is a clinical entity frequently found in everyday practice. Despite this, there are only a few indications to treat it. Unfortunately, even though the guidelines are clear, inappropriate antibiotic treatment is still offered and determines antimicrobial resistance and selection of extremely aggressive uropathogens. As we presented above, the screening and the antibiotic treatment of ABU are recommended only in pregnant women and in selected individuals who will have endourological procedures that can potentially determine the urothelial mucosa trauma. It remains that future studies could identify alternative methods and treatments, to better manage the patients with asymptomatic bacteriuria.

***Conflicts of interest and sources of funding***

*The authors declare no conflict of interest. No artificial intelligence automatically generated text was inserted in this manuscript, and no image was previously published in another journal or is under consideration of being published elsewhere. This research received no external funding.*

***Authors' contribution***

*Conceptualization, F.L.T.M and I.A.V., methodology, A-R.M., D.E.G., M.R.M., and A.E.B-S., software, A.M.S., M.R.M.., I.A.V., and F.L.T., validation, I.A.V., and M.R.M.., formal analysis, F.L.T., A-R.M., D.E.G., A.M.S., and A.E.B-S., investigation, F.L.T., I.A.V., and M.R.M., resources, F.L.T., and I.A.V., data curation, A-R.M., D.E.G., and A.M.S writing—original draft preparation F.L.T.M and I.A.V., writing—review and editing, F.L.T.M, D.M., A.E.B-S., and I.A.V., visualization, F.L.T.M and I.A.V.; supervision, I.A.V., and D.M.; project administration F.L.T.M and I.A.V.; funding acquisition, F.L.T.M. All authors have read and agreed to the published version of the manuscript.*

***Ethics approval and consent to participate***

*Not applicable.*

***Patient consent for publication***

*Not applicable.*

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